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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/341,009 08/25/99 WU

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023552
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HM22/0802

EXAMINER

ART UNIT	PAPER NUMBER
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1653
DATE MAILED:

16
08/02/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/341,009

Applicant(s)

Wu et al.

Examiner

Hope Robinson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on May 14, 2001.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 21 and 24-31 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 21 and 24-31 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- *See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892) 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 19) ☐ Notice of Informal Patent Application (PTO-152)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 20) ☐ Other:

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DETAILED ACTION

1. Applicant's response to the communication mailed April 10, 2000 in Paper No. 15 on May 14, 2001 is acknowledged. It is noted that applicants have further amended claims 21 and 24. It is also noted that applicants have asserted that the invention is directed to a method of treatment. Therefore, *in vitro* methods encompassed by the claims will not be examined as it pertains to a non-elected invention.

2. Applicant's response to the Office Action mailed July 21, 2000 in Paper No. 12 on January 17, 2001 is acknowledged. It is noted that applicant is requesting reconsideration and re-examination of claims 18-20. However, claims 18-20 were never examined on the merits as the claims are directed to a non-elected invention (as indicated in the prior office action, Paper No.10). Claims that are not elected or canceled cannot be examined on the merits, therefore, applicant's request cannot be granted.

3. Claims 21, 24, 30 and 31 have been amended. Claims 18-20 have been canceled. Claims 21 and 24-31 are pending.

4. The rejections under 35 U.S.C. 112, first paragraph and 103(a) have been withdrawn. The following grounds of rejection are or remain applicable :

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Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 21 and 24-31 remain rejected under 112, second paragraph as failing to distinctly point out the subject matter applicant regards as his invention.

Claim 21 is rejected as being indefinite because the claim recites “ a method for reversing the ongoing proliferation or activity or both of activated blood cells” without defining what activity is being reversed. Note that “proliferation” and “activity” are not equivalent terms therefore, the claim should recite the specific activity. Further, the claim is indefinite for reciting “capable of achieving”, because the words “capable of achieving” implies that there are times that this concentration will not be achieved and thus the desired results. Moreover, what is the endpoint or result of the method, since there are no steps indicating this. Claim 21 is also vague and indefinite because there is no indication in the method that it is a treatment of anything or any indicia of who the method will be administered to. Furthermore, the method does not provide any steps to indicate how to measure the claimed concentration. Is it measured in blood or interstitial fluids?

Claim 24 is indefinite because the claim recites “adding an immunosuppressive drug to the proteasome inhibitor and there is no indicia of the effect or what drug to use in this method step.

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Claim 26 is indefinite because the claim recites "results into activated blood cells apoptosis" instead of "results in..." (see also claim 27).

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 21 and 26-30 are rejected under 35 U.S.C. 102 (b) as being anticipated by Schreiber et al. (WO 96/32105, October 17, 1996) based on a method for reversing the ongoing proliferation **or activity** or both of activated blood cells (see claim 21).

Schreiber disclose a treatment which includes reversing, reducing or arresting the symptoms, clinical signs and underlying pathology of a condition in a manner to improve or stabilize the subject's condition (see page 81). Schreiber also disclose a method for treating inflammation, wherein the method includes administering to a subject an effective anti-inflammatory amount of a pharmaceutical composition containing a compound (lactacystin).

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Schreiber describes inflammation as a primary or secondary response to surgery (i.e. transplantation), infection etc. (see page 85). Also chronic or acute inflammation can result from transplantation rejection (i.e. tissue grafts, skin grafts, organ of any type etc.) or autoimmune diseases (see page 87).

In addition, Schreiber disclose that the preferred compounds and compositions include various lactacystin thioesters, and lactacystin β -lactone analogs, including the β -lactone itself (see claim 30). Schrieber further disclose the lactacystin in a concentration of $10\mu\text{M}$ which fits into the claimed range of 6 to $20\mu\text{M}$ as recited in claim 21 (see example 2 on page 94). As the claimed invention is directed to a method for reversing the ongoing proliferation or activity or both of activated blood cells and the claimed "activity" is not recited and Schrieber teaches the claimed compound at a concentration that is within the claimed range in a method to produce the same effect. Thus, as the claimed compound is taught by Schrieber, the result of inhibition of energy and oxygen by inhibiting the function of the mitochondria (claims 27-29) would be achieved because this an inherent property of the compound. Therefore, the limitations of the claims are met by this reference.

7. Applicant's response filed January 17, 2001 in Paper No. 13 has been considered but was not fully persuasive. The rejections under 35 U.S.C. 112, second paragraph and 102(b) remains.

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With regards to the rejection under 35 U.S.C. 112, second paragraph, applicant states that the claims have been amended to remove “action” which is now defined as proliferation or activity or both. This amendment to the claims instituted new grounds of rejection because the specific ongoing activity that the method reverses is not described and “activity” and “proliferation” are not equivalent terms (see reasoning above). Note that other grounds of rejections have been instituted as a result of the amendment to claim 21 for the reasons indicated above. The rejection over claim 24 remains because the method still does not recite the effect of the immunosuppressor and applicant’s response did not address this issue.

Regarding the rejection under 35 U.S.C. 102(b), applicant’s argues that the Schreiber reference does not provide any support to the fact that a proteasome inhibitor could reverse ongoing adverse reaction in activated blood cells. This argument is not convincing because Schreiber discloses the reversal of symptoms related to this type of inhibition. Note also that the claim recite “a method for reversing the ongoing proliferation or activity or both”, which makes the Schreiber reference relevant. Additionally, the applicant has stated on the record that the claimed invention is directed to “a method of treatment”, thus, the non-elected in vitro methods encompassed by the claims is have been withdrawn from consideration as noted above. Furthermore, the claimed method is incomplete as indicated above under the statute 35 U.S.C. 112, second paragraph, thus, the Schreiber reference is relevant as it teaches the claimed compound in a treatment method.

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With regard to the rejection under 35 U.S.C. 103(a), the rejection has been withdrawn as there is no motivation to add an immunosuppressant.

Art of Record

8. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Hess et al. (The Journal of Pharmacology and Experimental Therapeutics, vol. 281, no. 1, 1997). Hess teach the induction of T-cell inhibition via the synergistic effects of immunosuppressants such as FK506, rapamycin and cyclosporin A.

Armistead et al. (U.S. Patent No. 5,665,774, March 8, 1993). Armistead disclose immunosuppressive drugs to prevent or significantly reduce graft rejection in bone marrow and organ transplantations and for use in the treatment of a wide variety of autoimmune diseases in humans and other mammals. Armistead disclose a method of administering immunosuppressants FK-506, cyclosporin A and rapamycin to control or reverse chronic rejection of allografts in a transplantation patient.

Imajoh-Ohmi et al. (Biochemical and Biophysical Research Communications, vol. 217, No. 3, pages 1070-1077, 1995). Imajoh-Ohmi teach that the administration of lactacystin to cultured human monoblastic U937 cells resulted in apoptotic cell death of the U937 cells.

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Griscavage et al. (PNAS, vol. 93, pages 3308-3312, April 1996). Griscavage teaches that inhibitors of the proteasome pathway interfere with induction of nitric oxide synthase which is responsible for the production of NO by numerous cell types.

Conclusion

9. Applicant's amendment necessitated the new/modified ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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10. No claims are presently allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope Robinson whose telephone number is (703) 308-6231. The examiner can normally be reached on Monday-Friday from 9:00 am to 5:30 pm (EST).

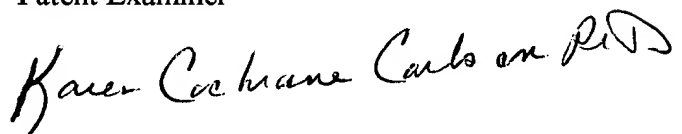
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher S.F. Low, Ph.D., can be reached at (703) 308-2923.

Any inquiries of a general nature relating to this application should be directed to the Group Receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted by facsimile transmission. The official fax phone number for Technology Center 1600 is (703) 308-4242. Please affix the examiner's name on a cover sheet attached to your communication should you choose to fax your response. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989).

Hope Robinson, MS 

Patent Examiner


KAREN COCHRANE CARLSON, PH.D.
PRIMARY EXAMINER